REMARKS

Applicants thank Examiner Canella for her time and helpful comments during a telephonic interview with the undersigned representative on September 7, 2006. The substance of the interview related to rejection of the claims under 35 U.S.C. § 103 in view of the cited documents, particularly, Sundberg et al. (*J. Am. Chem. Soc.* 117:12050-57 (1995)) and Becton Dickinson Acute Leukemia Phenotyping Kit. Possible claim amendments and arguments were discussed, but no agreement was reached.

Reconsideration of the present Application in view of the above Amendments and Request for Continued Examination enclosed herewith and the following remarks is respectfully requested. Applicants have hereby amended claim 1 and added new claims 24-27 to particularly point out and distinctly claim certain embodiments of Applicants' invention. Accordingly, upon entry of this amendment claims 1, 2, 18-21, and 24-27 are currently under examination. No new matter has been added to the application. Support for the amended claim and new claims may be found throughout the application, for example, at page 34, lines 12-16; page 35, lines 14-18; page 37, line 25 through page 38, line 1; page 45, lines 1-9; page 45, line 30 through page 46, line3; page 47, lines 21-22; page 56, lines 19-20; page 51, line 10; page 54, line 30 through page 55, line 1; and page 57, lines 22-30.

REJECTIONS UNDER 35 U.S.C. § 103

Claims 1, 2, 19, and 20, stand rejected under 35 U.S.C. § 103, allegedly for being obvious over Sundberg et al. (*J. Am. Chem. Soc.* 117:12050-57 (1995)) in view of the Becton Dickinson Acute Leukemia Phenotyping Kit (Becton Dickinson). The Action asserts that the presently claimed embodiment of Applicants' invention would have been *prima facie* obvious at the time of filing the instant application to use the antibodies taught by Becton Dickinson in an array described by Sundberg et al.

Applicants respectfully traverse this rejection and submit that the instant claims meet the requirements for nonobviousness. To establish a *prima facie* case of obviousness the Action must show that (1) the references teach or suggest all claim limitations; (2) the references provide some teaching, suggestion, or motivation to combine or modify the teachings of the prior

art to produce the claimed invention; and (3) the combined teachings of the references indicate that by combining the references, a person having ordinary skill in the art will achieve the claimed invention with a reasonable expectation of success. When rejection of claims depends upon a combination of prior art references, something in the prior art as a whole must suggest the desirability, thus the obviousness, of making the combination (*see In re Rouffet*, 149 F.3d 1350, 1355, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998)).

The present claims are directed, in pertinent part, to a method for identifying a leukemia or for identifying the propensity of developing a leukemia of T cell, B cell, or myeloid lineage in a human subject, comprising contacting a biological sample comprising leukocytes with an array of immunoglobulin molecules immobilized to a solid support. The array comprises 20 to about 1000 regions, wherein each region comprises immunoglobulin molecules that are specific for a distinct cell surface marker antigen. Binding of the immunoglobulin molecules to the cell surface marker antigen provides a pattern of expression on the leukocytes that distinguishes leukemias of T cell, B cell, or myeloid lineage, wherein the cell surface marker antigens are selected from the list in Table 4. The method further comprises determining the relative scale of the pattern of expression with which cell surface marker antigens have bound to the immobilized immunoglobulin molecules to establish a differential pattern of density of binding that identifies a leukemia that is of T cell, B cell, or myeloid lineage.

A person having ordinary skill in the art would not find the presently claimed embodiments of Applicants' invention obvious in view of the cited documents because each document, either alone or in combination, fails to teach each feature of the present claims. Neither Sundberg et al. nor Becton Dickinson teach a method for identifying a leukemia or for identifying the propensity of developing a leukemia of T cell, B cell, or myeloid lineage that comprises contacting a biological sample comprising leukocytes with an array of 20 to about 1000 immunoglobulins (*see, e.g.,* specification at page 35, lines 14-18; page 44, lines 24-30; page 45, lines 1-9; page 51, line 10; page 52, lines 1-2; page 61, lines 1-24; page 63, lines 21-24; and Tables 4, 6, and 7). The cited documents, alone or in combination, also fail to describe a method that comprises establishing the relative scale of the pattern of expression with which cell

surface marker antigens have bound to the immobilized immunoglobulin molecules to establish a differential pattern of density of binding that identifies the cell lineage of the leukemia.

Applicants submit, and the Action agrees, that Sundberg et al. fail to describe a method for detecting leukemia or any cancer. Sundberg et al. instead teach preparation of a simple array using a complicated method for attaching macromolecules to a support. Sundberg et al. describe binding *of only two* different antibodies to a flow cell. The Action asserts that Sundberg et al. teach only one example of a spatially localized array and teach that "higher resolution, allowing for a denser array, would be obtained by using thinner glass slides or printing on the front surface." However, Sundberg et al. fail to teach that increased resolution using the immobilization system described therein will result in an array comprising 20-1000 regions, which each have immunoglobulin molecules specific for a distinct cell surface marker antigen. Instead, and as previously made of record, Sundberg et al. teach that a limitation of the method described therein "is its reliance on serial rounds of photodeprotection and immobilization, which may *restrict* its application to the creation of *fairly simple arrays* of biomolecules (*see* Sundberg et al., at page 12056, second column, lines 11-14) (emphasis added). Thus, Sundberg et al. teach away from the claimed method that comprises contacting a biological sample with an array of 20 to about 1000 regions comprising immunoglobulin molecules that are immobilized to a solid support. Moreover, Sundberg et al. are silent regarding establishing a differential pattern of density of binding of the immobilized immunoglobulin molecules with cell surface marker antigens that are expressed on the cell surface of leukocytes in the biological sample. Accordingly, a person having ordinary skill in the art would have no reasonable expectation of successfully achieving the claimed methods.

The teachings of Becton Dickinson fail to remedy the deficiencies of Sundberg et al. Becton Dickinson fail to teach or suggest a method for identifying a leukemia or for identifying the propensity of developing a leukemia by contacting a biological sample with an array of 20 to about 1000 immunoglobulins that are immobilized on a solid support. Instead, Becton Dickinson teach a method of direct immunofluorescence staining and flow cytometry to determine the presence of up to ten (10) cell surface antigens (plus two control antigens) using sequential analysis of antibody/antigen pairs. Also, as conceded by the Action, Becton

Dickinson further fail to teach or suggest that a differential pattern of density of binding is obtained when cell surface marker antigens expressed on leukocytes in a biological sample are contacted with the array of immunoglobulin molecules.

Furthermore, neither cited document provides any requisite teaching, suggestion, or motivation to combine the teachings of either document or to modify the methods taught in either document to obtain Applicants' claimed methods. A person having ordinary skill in the art would not be motivated to increase the number of immunoglobulins/antigens described by Becton Dickinson to eliminate the expense of flow cytometry by modifying the teachings of Sundberg et al. to obtain the claimed methods because Sundberg et al. teach that their method is likely limited to simple arrays of biomolecules (*see, e.g.,* page 12056, first column). Sundberg et al. further teach that immobilization methods other than those described therein may not permit immobilization of different biomolecules to the same surface (*see* Introduction). Thus, Sundberg et al. suggest that any modification to the method described therein would render the method inoperable for its intended purpose.

Applicants further submit that the methods described and claimed in the present application fulfill a long-felt need in the art for identifying a leukemia or for identifying the propensity of developing a leukemia of T cell, B cell, or myeloid lineage using a plurality of different immunoglobulins in a single method. Prior to the filing date of this application, a person having ordinary skill in the art could attempt to determine the lineage of a leukemia only by performing sequential rounds of flow cytometry using a limited number of antibodies. Such methods have the disadvantages of high cost, length of time to perform the analysis, and the requirement for a highly skilled operator.

Therefore, Applicants submit that claims 1, 2, 18-21, and 24-27 meet the requirements for nonobviousness under 35 U.S.C. § 103. Applicants submit that the Action has failed to establish a *prima facie* case of obviousness and request that this rejection be withdrawn.

Claims 1, 2, 18, 19, 20, and 22 stand rejected under 35 U.S.C. § 103, allegedly for being obvious over Sundberg et al. in view of Becton Dickinson and further in view of Paul (*Fundamental Immunology* (1993) page 460). The Action asserts that Paul teaches the

advantages of using polyclonal antibodies instead of monoclonal antibodies for diagnostic methods and that a person having ordinary skill in the art would have found obtaining Applicants' claimed method obvious by combining the teachings of Sundberg et al., Becton Dickinson, and Paul.

Applicants respectfully traverse this rejection and submit that the claimed methods are nonobvious as required under 35 U.S.C. § 103. Applicants refer the Examiner to the discussion above that Sundberg et al. in view of Becton Dickinson fail to teach or suggest each feature of the claimed method for identifying a leukemia or for identifying the propensity of developing a leukemia of T cell, B cell, or myeloid lineage and further fail to provide any motivation, teaching, or suggestion to combine or modify the teachings of either or both documents to obtain successfully the presently claimed embodiments of Applicants' invention. Paul fails to remedy the deficiencies of Sundberg et al. and Becton Dickinson.

Applicants respectfully disagree with the Action that Paul provides any motivation, teaching, or suggestion to use either monoclonal antibodies or polyclonal antibodies preferentially in the claimed method. Paul fails to teach or remotely suggest a method for identifying a leukemia or for identifying the propensity of developing a leukemia of T cell, B cell, or myeloid lineage. Paul fails to teach or suggest a method that comprises contacting a biological sample comprising leukocytes from a human subject with an array of immunoglobulins, wherein the array comprises 20 to about 1000 regions that each comprise immunoglobulin molecules specific for a distinct cell surface marker antigen. Paul further fails to teach or suggest that either monoclonal antibodies or polyclonal antibodies may be used in the claimed method. Paul teaches that polyclonal sera may have an advantage for use in certain immunoassay techniques such as immunoprecipitation, which may benefit from the multivalency of polyclonal antisera. Applicants submit that Paul provides nothing more than a cumulative reference that monoclonal antibodies and polyclonal antisera have different characteristics that a person skilled in the art may wish to consider when contemplating use of an immunoglobulin source.

Applicants therefore submit that the present claims are nonobvious over Sundberg et al. in view of Becton Dickinson and in further view of Paul and respectfully request that this rejection be withdrawn.

Claims 1, 2, and 19-22 also stand rejected under under 35 U.S.C. § 103, allegedly for being obvious over Sundberg et al. and Becton Dickinson and in further view of Terstappen et al. (U.S. Patent No. 6,265,150). The Action asserts that Terstappen et al. teach a method of rapidly obtaining human antibodies against known and novel surface antigens and that a person having ordinary skill in the art would have been motivated to use a library of phage particles expressing antibody fragments as a renewable source of antibody fragments for use in the claimed method.

Applicants respectfully traverse this rejection and submit that the Action has failed to establish a *prima facie* case of obviousness and that the presently claimed method is nonobvious over Sundberg et al. and Becton Dickinson in further view of Terstappen et al. Applicants refer the Examiner to the discussion above that Sundberg et al. in view of Becton Dickinson fail to teach or suggest each feature of the claimed method for identifying a leukemia or for identifying the propensity of developing a leukemia of T cell, B cell, or myeloid lineage and further fail to provide any motivation, teaching, or suggestion to combine or modify the teachings of either or both documents to obtain successfully the presently claimed embodiments of Applicants' invention. Terstappen et al. fail to remedy the deficiencies of Sundberg et al. and Becton Dickinson.

Terstappen et al. fail to teach or remotely suggest a method for identifying a leukemia or for identifying the propensity of developing a leukemia of T cell, B cell, or myeloid lineage. Terstappen et al. fail to teach or suggest a method that comprises contacting a biological sample comprising leukocytes with an array of immunoglobulins, wherein the array comprises 20 to about 1000 regions that each comprise immunoglobulin molecules specific for a distinct cell surface marker antigen. Terstappen et al. further fail to teach or suggest that immunoglobulin fragments obtained from phage libraries may be used in the claimed method. Applicants submit that Terstappen et al. provide nothing more than a cumulative reference from

the art describing one of several methods practiced in the art at the time the present application was filed to screen and identify immunoglobulin fragments that specifically bind to an antigen of interest.

Applicants therefore submit that the Action has not established a *prima facie* case of obviousness of the presently claimed subject matter over Sundberg et al. in view of Becton Dickinson and in further view of Terstappen et al. Applicants further submit that the present claims satisfy the requirements for nonobviousness under 35 U.S.C. § 103, and request that all rejections of the claims be withdrawn.

Applicants respectfully submit that all claims in the application are allowable. Favorable consideration and a Notice of Allowance are earnestly solicited. In the event that the Examiner believes a teleconference will facilitate prosecution of this case, the Examiner is invited to telephone the undersigned at 206-622-4900.

Respectfully submitted,

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